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THE INHERITANCE OF EPILEPSY AND OF WALTZING IN *PEROMYSCUS**

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INTRODUCTION

BEHAVIOR defects, roughly classified as epilepsy and as waltzing, occur in several races and species of *Peromyscus* as well as in many other kinds of mammals. All of these defects known to occur in *Peromyscus* are herein described and their mode of inheritance discussed. The data previously published by Dice (1935: 27–34) on the inheritance of waltzing and of epilepsy in *Peromyscus* are combined in this report with all the new data available up to June, 1937. The epilepsy which occurs in *Peromyscus* is a particularly important character for study, because it is closely similar to certain types of epilepsy in man.

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STOCKS

The stocks of mice used in this study are as follows:

Peromyscus maniculatus artemisiae, Lyons Ferry, Franklin County, Washington. Collected by L. R. Dice, 1928.

Peromyscus maniculatus artemisiae, Palouse Falls, Franklin County, Washington. Collected by Arthur and Ruth Svihla, 1931.

Peromyscus maniculatus artemisiae, Polson, Lake County, Montana. Collected by L. R. Dice, 1934.

Peromyscus maniculatus bairdii, Alexander, Franklin County, Iowa. Collected by Paul Moody, 1926.

Peromyscus maniculatus osgoodi, Glen Ullin, Morton County, North Dakota. Collected by L. R. Dice, 1934.

Peromyscus maniculatus rufinus, Deadman Flat, Coconino County, Arizona. Collected by G. W. Bradt, A. J. Nicholson, and A. M. Stebler, 1932.

Peromyscus polionotus rhoadsi, Leesburg, Lake County, Florida. Collected by C. C. Goff, 1934.

Peromyscus boylii rowleyi, Summerhaven, Pima County, Arizona. Collected by L. R. Dice, 1932.

Peromyscus eremicus eremicus, Carrizozo, Lincoln County, New Mexico. Collected by G. W. Bradt, 1929.

METHODS AND APPARATUS

In order to secure a standardized stimulus a key shaking machine was developed, run by a sewing-machine motor, which could shake keys at two speeds. The lower speed gave a gentle shake to the keys, and the next speed shook them vigorously. The testing enclosure was 3 feet square, with sides of galvanized iron, 18 inches high. The lower 3 inches of the enclosure were padded with cotton, so that the mice, when excited, would not injure themselves against the hard side walls.

TYPES OF WALTZING IN *PEROMYSCUS*

Waltzing occurs in six distinct stocks of *Peromyscus* kept at the Laboratory of Vertebrate Genetics of the University of Michigan. These stocks represent three species and two species-groups. In four of these stocks waltzing is not associated with epilepsy.

Waltzing in bairdii

The waltzing behavior of *Peromyscus maniculatus bairdii* is very similar to that of the Japanese waltzing mouse. When stimulated by a loud noise or by being put into a new cage, *bairdii* waltzers turn circles very rapidly, sometimes so fast that they seem to be pivoting on one foot. They differ from the Japanese waltzers in having nervous movements of the head when waltzing and sometimes when not waltzing. In this respect they are more nearly like the shakers of Lord and Gates (1929: 435) and of Dobrovolskaia-Zavadskaia (1928: 476) and the circlers described by Laanes and MacDowell (1936: 68). Waltzers of the *bairdii* stock circle both clockwise and counter clockwise, and an animal may change the direction of circling two or three times during one waltz.

The characteristic movements of the waltzers are evident at the time of weaning, and most animals continue to show the waltzing behavior until death. They are perhaps more vigorous in their waltzing when young, but even old animals are highly active when stimulated.

In order to test the hearing of the waltzing animals they were put singly into a testing enclosure, and a steel forceps was struck on a glass tumbler held just outside the enclosure so that the mice could see no movement of the hands of the experimenter. At this sudden sharp noise, most of the mice that could hear responded with a twitch of the ears.

The waltzers of the subspecies *bairdii* seem to be able to hear until they are very old, but there is much individual difference in the age at which they cease to respond to sounds. The oldest animal tested which still gave the characteristic ear twitch was 27 months of age; another waltzer failed to give the twitch at the age of 18 months. The older animals require a louder noise before they respond than do the younger ones. Dice (1935: 29), on the basis of insufficient numbers of observations, supposed that *bairdii* of all ages were able to hear.

Waltzing in *P. m. bairdii* from Alexander, Iowa, is inherited as a simple Mendelian recessive character. From matings of waltzer by waltzer, however, three animals were produced which could not be made to waltz, though they were tested several times (Table I). The most probable explanation for the occurrence of these normal animals is that they are normal overlaps, that is, they do not show phenotypically their genotypic character. Since both parents were waltzers, all the young produced should have been homo-

TABLE I

INHERITANCE OF WALTZING (w) IN *P. MANICULATUS BAIRDII* FROM ALEXANDER, IOWA

Matings	No. of Young	Types Produced		Expected Types		Difference from Expected
		Waltzer	Normal	Waltzer	Normal	
Within the stock						
ww × ww	27	24	3	27	0	3
ww × Ww	53	26	27	26.5	26.5	......
After outcrossing						
ww × WW	65	0	65	0	65	......
Ww × Ww	155	22	133	39	116	17

zygous for the waltzing gene. An attempt was made to test these aberrant normally reacting animals to determine whether or not they were homozygous for the waltzing gene. Unfortunately, the female died before she bore any young, but one of the males when mated to a waltzing female produced two waltzing young. The number is too small to prove that he was homozygous for the waltzing gene.

Waltzers of the *bairdii* stock were outcrossed to a stock of *P. m. artemisiae* from Palouse Falls, Washington. In the F_1 generation 65 normal animals were produced. In the F_2 generation 22 waltzers and 133 normals were produced. The waltzers numbered 17 less than expected, probably because of the outcross, since animals of a different subspecies and from a different locality may have different modifying factors. Dice (1935: 28) and McPheters and Little (1935: 157) also found deficiencies after an outcross.

The extracted waltzers in the F_2 generation of *P. m. bairdii* from Alexander, Iowa, by *P. m. artemisiae,* from Palouse Falls, Washington, were then crossed with waltzers of the stock of *P. m. artemisiae* from Palouse River, Washington. Twenty-one normal individuals were produced, which shows that the waltzing of *bairdii* and of *artemisiae* is caused by different hereditary factors. If the two waltzing characters had been genetically identical, according to expectation all of the young should have been waltzers.

On the basis of the data presented above, waltzing in *P. m. bairdii* is caused by a single recessive gene mutation. There are, however, some normal overlaps, probably caused by modifying factors. The waltzing in *P. m. bairdii* and *P. m. artemisiae* is genetically distinct.

Waltzing in eremicus

The most vigorous of the *Peromyscus* waltzers were those of the *eremicus* stock from Carrizozo, New Mexico. The waltzing movements in *eremicus* are too fast to be followed by the eye, and a motion picture camera at 64 frames per second (1/108 second exposure for each frame) does not stop the motion. These waltzers seldom make large circles, and I have never seen one waltz in a figure 8, as the *bairdii* and Japanese waltzers sometimes do. All animals seem to be able to waltz in either direction.

Head movements are more pronounced in *eremicus* waltzers than in those of any other stock. A few individuals have been found which exhibited the peculiar head movements but did not waltz. Dice (1935: 26) found that at least one of these animals was heterozygous for the waltzing character. The waltzers continue to perform throughout life, and old waltzers are just as vigorous as young ones.

The *eremicus* waltzers seem to lose their hearing sometime between the first and second month of life. Most of them exhibit an ear twitch at the sound of a sharp noise when they are 1 month old, but I have never tested a waltzing animal of the *eremicus* stock 2 months of age or older which showed the ear twitch.

The nonwaltzers, including animals heterozyogus for waltzing, with only one exception, gave an ear twitch whenever tested. These nonwaltzers were tested for hearing at ages ranging from 1 to 27 months. The one deaf nonwaltzer was 23 months old; breeding tests indicated that this animal was homozygous for the waltzing character but did not show the typical movements of the waltzers.

Waltzing in *eremicus* is inherited as a simple Mendelian recessive character. In all matings the actual types produced are as close as is possible to the expected types (Table II). The results of the matings indicate that waltzing in *P. e. eremicus* is caused by a single recessive gene. Only one normal overlap has been found.

It is impossible to determine whether waltzing in *eremicus* is identical with or distinct from the waltzing which occurs in *bairdii* and *artemisiae,* because members of the *eremicus* group of *Peromyscus* do not breed with members of any other group.

TABLE II

INHERITANCE OF WALTZING (w) IN *P. EREMICUS EREMICUS* FROM CARRIZOZO, NEW MEXICO

Matings	No. of young	Types Produced		Expected Types	
		Waltzer	Normal	Waltzer	Normal
ww × ww	30	30	0	30	0
ww × Ww	113	57	56	56.5	56.5
Ww × Ww	31	8	23	7.75	23.25
WW × WW	69	0	69	0	69

Waltzing in maniculatus Piebald Stock

Waltzing has also occurred in a mutant *maniculatus* stock of piebald animals of unknown ancestry. Waltzing in the piebald animals is often spontaneous and is always accompanied by a large amount of nervous movement of the head and body. In these movements piebald waltzers resemble markedly the waltzers of the *eremicus* stock. No data have been secured on the mode of inheritance of the waltzing character in the piebald *maniculatus* stock.

Summer (1932: 9) found a waltzing animal in a mutant *maniculatus* stock of albinos crossed with pallids, but the mode of inheritance of the character was not determined.

Waltzing in rhoadsi

The waltzing behavior in *Peromyscus polionotus rhoadsi* was first noted by Frank H. Clark. These waltzers often need very little stimulation and sometimes waltz quite spontaneously. The movements are usually not so vigorous as are those of *bairdii* and *eremicus* waltzers, but occasionally an animal may waltz faster than do the *bairdii* waltzers and almost as fast as the *eremicus* waltzers. There are no nervous head movements.

The waltzers of the *rhoadsi* stock have only recently been discovered, and the study of the inheritance of the character has just been started. The waltzing behavior, however, seems to be inherited as a single recessive. Only one pair of animals of the *rhoadsi* stock carrying the defect has been fertile up to the present time, and this pair consists of two normals both heterozygous for the waltzing character. Thus far sixteen young have been produced, of which twelve are normal and four are waltzers. These are exactly the expected numbers of the two types for a simple Mendelian recessive character.

TYPES OF EPILEPSY COMBINED WITH WALTZING IN *PEROMYSCUS*

In two stocks of *Peromyscus maniculatus artemisiae* both epilepsy and waltzing occur. In the stock from Palouse River the two defects may or may not have originated simultaneously, but in the stock from Polson they first appeared in the same animal.

Epilepsy and Waltzing in artemisiae from Palouse River

The waltzing character in the Lyons Ferry stock of *artemisiae* was first noted after several generations of inbreeding in the laboratory. According to Dice (1935: 25–26) the waltzing gene was probably present in the wild population, and through inbreeding in the laboratory homozygous recessives were produced.

The epileptic character first appeared among the offspring of an outcross of the waltzing Lyons Ferry stock to a normal stock of the same subspecies, *artemisiae,* from Pullman, Washington. An F_1 animal of this cross was backcrossed to a waltzer from Lyons Ferry, and among the young produced the first epileptic animal was noted. The factor for epilepsy must have been present in the stock from Lyons Ferry, because, since the character is recessive, the epileptic animal must have received one factor for epilepsy from each parent. Dice earlier (1935: 31) suggested that epilepsy may have come in from the Pullman stock, but no other cases of epilepsy were observed in the nonwaltzing Pullman animals, and any recesssive gene in the Pullman stock would not have been manifest as the result of a backcross to Lyons Ferry animals.

The stock containing both epilepsy and waltzing, which resulted from the outcross of the Lyons Ferry to the Pullman stock, was again outcrossed to normal *artemisiae* from Palouse Falls, a station only 5 miles distant from Lyons Ferry. The stock that still carried both epilepsy and waltzing from this outcross, has for convenience been called the Palouse River stock.

The waltzing behavior of *artemisiae* is very similar to that of the other forms of *Peromyscus* described above. The *artemisiae* waltzers, however, usually require some form of external stimulation before they will exhibit the characteristic circling movements. They may be stimulated by a touch on the tail, by a loud or sudden noise, or by putting them into a new cage. The usual stimulus employed in the Laboratory has been the sound made by the shaking of a bunch of keys. The waltzing movements of *artemisiae* are as rapid as those of *bairdii,* but they are less rapid than those of *eremicus.*

When an epileptic mouse is stimulated it usually assumes a crouching position with muscles tense, ears drawn back, and nose pointed forward. This reaction is followed by a period in which the animal dashes wildly about the cage; thereafter, the animal usually falls over in an epileptic seizure. It is my practice to stop the stimulus as soon as dashing begins, so that the seizure occurs without the stimulus.

The change from the crouching position to the dashing phase is very sudden, and might be termed explosive. In a flash the mouse is up and running madly and utterly at random about the cage. This lasts 1 to 15 seconds after the stimulus has ceased. The mouse tends to run in a straight line, but if there is some obstruction, it will probably bump violently into it. By bumping their heads against the sides of the metal enclosure in which they are tested, several mice have suffered such severe trauma, causing cerebral hemorrhage, that they have died almost immediately. Normal animals have excellent control over their movements and are very agile in avoiding or jumping over obstructions.

An epileptic seizure often follows the period of dashing. In a typical seizure the animal falls on its side, and for a few seconds there are rapid spasmodic movements of its four legs. These movements may be compared with the clonic phase of the human epileptic seizure. After a few seconds of these motions the hind legs are brought close to the body, and then gradually and slowly they are extended straight backward. At the same time, the forelegs are brought close to the body and meet or cross over the thorax of the mouse. At this time the mouse has an appearance of tenseness in every muscle of its body, from its open mouth to its extended legs and widely spread toes. This stage resembles in a very marked way the tonic phase of the human epileptic seizure. Respiration seems actually to cease for a moment, and when it is resumed, the animal takes five or six deep gulps of air through its mouth. With each intake of air, the mouse has a spasmodic movement of its whole body. After this beginning, breathing continues at a somewhat faster than usual rate.

At this time, which is usually 15 to 20 seconds after the onset of the seizure, the animal begins to relax, and the legs are drawn up into a bent position. The animal still lies on its side, perfectly quiet except for its regular breathing, and with its eyes closed as in sleep. This period of the seizure may last 30 seconds to 25 minutes, during which the mouse may be picked up in the hand, and it will stay in any position in which it is placed. After this the mouse gradually turns over until it is right side up, when it slowly walks away. If undisturbed, the mouse will seek a corner and go to sleep.

The total epileptic reaction of dashing and seizure, depending on the severity of the seizure, lasts from 2 to 30 minutes. Sometimes a mouse will die during a particularly severe seizure. When death occurs it comes just after the extension of the legs; the animal assumes the tense position but does not recover from it.

Some mice never have as severe a seizure as that just described; these may have a milder form which I have called a bouncing type of seizure. Other mice may have a severe seizure at one time, and the less severe bouncing type at another time.

The bouncing type of seizure has its beginning in exactly the same way as the complete seizure. The stimulus as usual is stopped as soon as dashing begins. After a period of dashing, the mouse falls over on its side, but it is able to get up again almost immediately. It draws up its forelegs, stands almost upright, and bounces on its bent hind legs. Its forelegs may touch the floor occasionally, but usually the bouncing is done almost completely on the hind legs. The mouse may fall over several times while in this condition, but it immediately bounces up again. The mouth of the mouse is open during the bouncing and usually a series of squeaks are emitted. After 5 to 20 seconds most of the mice in this condition will take hold of the cotton which surrounds the tin enclosure in which they are tested; they hang along the cotton with their feet or teeth for several minutes until they are able to walk away.

Another type of epileptic behavior which most of these defective mice will demonstrate at some time or other during their lives is what I have called a stupor. After the dashing phase, the animal comes to a stop and lies flat on its undersurface for several seconds or for several minutes. It looks and acts as though it were recovering from a seizure, though no seizure actually has occurred. It will remain in any position in which it is placed.

A still less severe form of epileptic behavior is the semistupor. After a period of dashing, the animal comes to a stop and lies flat as in stupor, but in this state the animal is capable of movement. It can be touched easily but cannot be handled. When disturbed, it moves a few steps away, but it cannot make fast or extensive movements. This condition usually lasts from several seconds to several minutes.

Occasionally, there is no further reaction to the stimulus other than dashing. This often occurs in older animals that do not react as readily as they did earlier in life, or when only a short duration of the stimulus has been given.

Dashing, semistupor, stupor, bouncing seizure, complete seizure, and death during seizure are undoubtedly only varying types of response based on a single inherited factor. They are listed here in order of increasing severity.

Many mice of the *artemisiae* stock exhibit both the epileptic and the waltzing characters. An animal with both epilepsy and waltzing may exhibit any of the types of behavior described above, usually, with some circling movement. The waltzing movements in *artemisiae*, as mentioned above, are very similar to those of *bairdii* waltzers.

When an epileptic waltzer is stimulated, the mouse generally assumes a crouching position, after which it suddenly and rapidly waltzes. At first the waltzing is in very small circles, but as it continues the circles become larger until the mouse is no longer waltzing but is dashing. After this phase there may be either a seizure, a stupor, or any of the other typical behavior patterns of the epileptic mice. If no stupor or seizure ensues the animal may waltz again after the dashing, or if this is followed by a stupor or seizure, it may waltz following its recovery from the abnormal state. Sometimes, during a bouncing seizure, an epileptic waltzer will bounce in circles.

DIFFERENCES IN REACTION WITH AGE.—The severity of the reaction of *artemisiae* epileptic mice varies with age. As a mouse becomes older, it usually requires more and more stimulation before it exhibits epileptic behavior. Some mice which have had seizures at the age of 1 or 2 months, merely go into a stupor when stimulated at the age of 4 or 5 months. A month or two later, they may merely run around nervously while the keys are being shaken, and even after prolonged stimulation they may not dash or have a seizure. Still later in life the epileptic mouse may sit perfectly still during the stimulus, and in no apparent way does its behavior differ from that of a normal mouse in the same situation.

The earliest age at which any *artemisiae* has waltzed is 11 days, and the youngest mouse to be recorded for dashing and epileptic seizure was 13 days old.

About half the epileptic and epileptic waltzing mice give the most severe reaction to the stimulus when 1 month old. The other half of the mice give the most severe reaction at ages varying from 2 to 10 months. The average age for the most severe reaction for all the mice which I have tested is 2.1 months.

There is no significant difference between the average age at which the mice cease to waltz and the ages at which they stop dashing (Table III).

TABLE III

AGE IN MONTHS AT WHICH MICE CEASE TO SHOW ABNORMAL BEHAVIOR. *P. MANICULATUS ARTEMISIAE*, PALOUSE RIVER, WASHINGTON

Type of Reaction	Number of Individuals	Average Age	Youngest Age	Oldest Age
Dashing	219	3.79 ± .18	1	15
Waltzing	120	3.48 ± .22	1	14
Seizures	88	2.64 ± .23	1	11

The average age at which a mouse has its last seizure is somewhat less, probably because, except for special work, no attempt is made to induce a seizure every time an animal is tested, for there is risk of death during the seizure.

The reactions of epileptics and waltzers of the stock of *artemisiae* thus vary with the age of the mouse. After reaching a maximum at the age of about 2 months, the reactions gradually become less severe or require more stimulation for their demonstration, until finally old epileptics and waltzers show behavior characteristics not different from those of normal mice.

Effect of differences in intensity of stimulus.—In order to determine whether an increased stimulus would cause a more prompt or more severe response in the epileptics and waltzers of the *artemisiae* stock, several mice were tested at the various speeds of the key-shaking machine. The mice were tested weekly, with the fast and slow speeds alternately.

In almost every test it was found that the mice reacted much sooner to the fast speed than they did to the slow speed. Some mice which reacted only after prolonged stimulation at the fast speed showed no abnormal behavior at all when the machine was run at the slow speed.

An example of the difference in reaction produced by the two speeds of the machine is given by the series of reactions of an epileptic waltzer, ♂29827. At the fast speed this mouse waltzed very rapidly in small circles as soon as the machine was started; after the keys had been shaken for 7 seconds, he dashed. The next week, when the machine was run at the slow speed, he waltzed as soon as the machine started, but for only 5 seconds; he then sat in the corner with no further response though the stimulus was continued for 2 minutes. The following week he again waltzed as soon as the machine was started at the fast speed, and dashed after it had run 10 seconds.

Waltzing, which the slow speed is sufficient to impel, is always produced by less stimulation than is necessary to bring on an epileptic seizure. The epileptic behavior of these mice is brought on either by a very long duration of the slow speed or by a more vigorous stimulus.

Absence of an immune period.—Lush (1930: 243) found that after an epileptic goat had had one seizure, it could not be induced to have another before a period of at least 30 minutes. Thus there seemed to be an immune period directly after the seizure.

In order to discover whether *Peromyscus* had such an immune period following a seizure, several mice were tested again immediately after they had recovered from a first reaction. In almost every instance, they could be induced to have another seizure or at least another dashing response immediately after recovery from the first seizure. In *Peromyscus,* moreover, the stimulation seemed to be cumulative, since the second response usually required less stimulation for its manifestation than did the first.

Absence of sex difference.—There seems to be no significant difference in the behavior of the two sexes with regard to epilepsy or waltzing. Of the epileptic nonwaltzing animals, twelve females and sixteen males always reacted promptly, and six females and eight males always required a large amount of stimulation to induce the abnormal behavior. In the epileptic waltzing group, fourteen females and twenty-one males always responded promptly to stimulation, and five females and four males always required much stimulation.

Of the epileptic nonwaltzing animals which sometimes reacted promptly and sometimes required prolonged stimulation, twelve were females and six were males. Of the epileptic waltzers which gave varied responses, eight were females and nine were males.

The average ages at which these mice cease to demonstrate their abnormal behavior is 3.8 months for the females and 3.9 months for the males.

Variation in individual responses.—Not only are the reactions of different mice exceedingly variable, but the reactions of each individual mouse vary from time to time. Besides the regular monthly testing of all the affected animals several mice were tested with the same stimulus once each day for thirty days.

It was found that among those *artemisiae* tested every day which exhibited both the epileptic and waltzing type of behavior waltzing occurred on an average of twenty-four out of thirty times. As an example of the amount of variation in epileptic behavior one mouse dashed after less than 25 seconds of stimulation on twenty-two of the thirty times tested; five times it required more than 25 seconds of key shaking before it exhibited the dashing behavior; and three times it could not be induced to dash at all, though the stimulus was continued for 90 seconds. This animal did not have a seizure on any of the thirty times tested, though it went into a stupor five times.

Another example of the variability of reaction is the record of ♀30903, which on 21 days dashed with a stimulation of less than 25 seconds, but which required more than 25 seconds of stimulation on 8 days. Once it did not dash at all, though the stimulus was continued for 100 seconds. This mouse was also a waltzer, though it waltzed only twenty of the thirty times tested.

Not all mice are as variable in the expression of the epileptic character as the two described above. One mouse, ♂30904, which was tested for 30 days, exhibited the dashing behavior twenty-nine times after less than 25 seconds of key shaking; only once did it require more than 25 seconds of stimulation in order to evoke the response.

Variation which is not caused by age or intensity of stimulus is also apparent in the animals tested once each month. One such mouse, ♀30053, when a month old, dashed after a stimulation lasting 25 seconds. At 2 and at 3 months old she did not respond, though the key-shaking machine was run for 90 seconds each time. When 4 months old she dashed and had such a severe seizure that she died, although the stimulus was continued only 5 seconds.

Of 121 mice which reacted three times or more when tested with the same stimulus, twenty-eight epileptic nonwaltzers and thirty-five epileptic waltzers always responded promptly to the stimulus, nine epileptic nonwaltzers and fourteen epileptic waltzers always required a large amount of stimulation in order to evoke a response, and eighteen epileptic nonwaltzers and seventeen epileptic waltzers varied in their reactions, sometimes responding readily and at other times requiring much stimulation.

The variability in the reactions of all the mice mentioned above is not caused by age differences nor differences in the intensity of stimulus, but is probably due to a difference in the physiological condition of the animal at the time of testing.

DEAFNESS.—Many of the older epileptic and waltzing animals in the stock of *artemisiae* from Palouse River are deaf. The onset of deafness in these mice seems to be gradual. Many mice which have been found to give a vigorous ear twitch at the sound of a sharp noise one month may give a very slight twitch the next month, and no response the third month. The average age at which a defective mouse of this stock becomes totally deaf is 6.8 ± 0.5 months.

Of 143 animals which no longer showed any epileptic or waltzing behavior, it was found that seventy-three could hear, and sixty-one were deaf. The oldest age at which any mouse has continued to hear is 16 months. The correlation coefficient for the age at which these animals no longer hear and the age at which they no longer react to the stimulus is 0.63.

Because epileptic animals can be stimulated only by loud or sharp noises, and because almost any noise long continued will cause the epileptic reactions, it seems that hearing must be related in some way to the expression of the epileptic character. Moreover, the onset of deafness, in mice which become deaf, occurs at almost the same age as that at which they no longer demonstrate any abnormal reactions.

SELECTION LINES.—Selection lines were formed in order to determine whether or not mice with prompt reactions would give rise to offspring with similar responses, and whether or not mice with slow reactions would have corresponding offspring.

The mice were divided arbitrarily into two classes: (1) those which dashed after 25 seconds or less of stimulation, or had a seizure after 40 seconds or less, and in which the reactions continued until the mice were at least three months of age; and (2) those which dashed after a stimulation of more than 25 seconds or had a seizure after more than 40 seconds, and in which seizures lasted during only 1 or 2 months of the animal's life. The animals with prompt reactions were designated as high grade, and those with slow reactions as low grade. All the abnormally reacting animals were graded as high-grade epileptic nonwaltzers, low-grade epiletic nonwaltzers, high-grade epileptic waltzers, or low-grade epileptic waltzers.

The data for offspring of the high-grade epileptic nonwaltzing parents in the first selected generation are given in Table IV. The majority of the young produced were of the type of the parents, though animals of other types were produced also, because at least some of the parents were heterozygous for other types of behavior.

In the first selected generation of the low-grade epileptic nonwaltzing

TABLE IV

SELECTION LINES FOR VARIOUS TYPES OF BEHAVIOR IN *P. MANICULATUS ARTEMISIAE* FROM PALOUSE RIVER, WASHINGTON

Parental Type	Fertile Pairs	Offspring					
		High-Grade Epil.	Low-Grade Epil.	High-Grade Epil. Waltzer	Low-Grade Epil. Waltzer	Non-epil. Waltzer	No Reaction
High-grade epileptic nonwaltzer	5	52	16	13	4	1	5
Low-grade epileptic nonwaltzer	5	9	9	2	5	0	2
High-grade epileptic waltzer	5	3	1	21	5	1	0
Low-grade epileptic waltzer	3	3	3	4	13	2	0

line, fourteen low-grade and eleven high-grade young were produced. The high-grade epileptic waltzing parents produced thirty-one offspring, of which twenty-one were of the type of the parents. The low-grade epileptic waltzing parents produced twenty-five offspring, of which thirteen were of the same type. No second generation is available for any of the selection lines.

The majority of the offspring of the first selected generation in each of the selection lines exhibit the same type of reactions as the parents. Although the numbers are small and there are both low- and high-grade young produced from both high- and low-grade matings, there seems to be a tendency toward the perpetuation of the line. In the first generation of selected animals, the high-grade type of behavior has bred more nearly true than has the low-grade type.

RESPONSE TO OTHER STIMULI.—Several methods of stimulation other than the shaking of keys were tried in order to induce epilepsy in *artemisiae,* but because of lack of time and equipment very little research along this line has been undertaken.

Some mice were tested with an electric doorbell placed directly under the table beneath the testing enclosure. Epileptic mice responded in exactly the same manner as to the keys, but it was necessary to ring the bell a longer time in order to induce the response. A policeman's whistle, attached to a compressed air supply, was blown within 10 inches of the mice. The epileptic mice responded, but, as with the doorbell, a greater duration of the stimulus was required. The high tones of a piccolo were tried, to determine whether a shrill high note would cause the response, since the sharp, high sounds of the jingling keys might be the causative agent in evoking it. No epileptic behavior was exhibited in response to this stimulus.

Several epileptic mice of this stock were placed in the smoke jar which is used to stimulate the *rufinus* type of epilepsy (see pp. 20–21), but the smoke caused no reaction in these mice. An electric grid was arranged so that the mice could not escape from it, and a mild current was run through it. The current was strong enough to make the mice jump, but not strong enough to injure them in any way. Although the epileptic mice jumped about considerably, their actions did not differ from those of normal mice placed in the same situation.

Almost all sound stimuli were successful in causing epileptic reaction, but no other type of stimulation which we have tried has caused abnormal behavior in *artemisiae.*

AUTOPSY REPORT.—An epileptic mouse, which had died in a seizure, was kindly autopsied immediately after death by Dr. Konstantin Lowenberg, of the State Psychopathic Hospital at Ann Arbor. His examination revealed no abnormality in the brain either macroscopically or microscopically.

EFFECT OF SODIUM-FREE DIET.—Epilepsy and waltzing in *Peromyscus* bear a very marked resemblance to Ménière's syndrome complex in man. Persons suffering from Ménière's disease have markedly fewer and less severe seizures when on a sodium-free diet (Furstenburg, Lashmet, and Lathrop, 1935: 267). Several high-grade epileptic *Peromyscus* waltzers were put on a sodium-free diet for 30 days and were tested at weekly intervals during this time. While on the diet there was no change in the severity of the reaction or in the duration of stimulation needed to induce the reactions.

INHERITANCE OF EPILEPSY AND WALTZING IN *ARTEMISIAE.*—Waltzing, considered apart from epilepsy, is obviously recessive in inheritance in the Palouse River mice. Although the data given in Table V do not fit perfectly into the ratio for a simple Mendelian recessive character, yet the results seem to correspond more closely to this than to any other ratio which one may apply.

In the matings of waltzer by waltzer, theoretically all the young produced should have been waltzers. The apparent normalcy that we have found may be due to an error of classification, or else the twelve mice of the normal class did not show phenotypically their genotypic waltzing character. At least one mouse was proved by breeding to be a normal overlap, that is, it was genotypically homozygous for the waltzing character but did not waltz. The percentage of 14.4 of normal overlaps for waltzing was found by the formula

$$\frac{\text{Expected waltzers} - \text{Observed waltzers}}{\text{Expected waltzers}} \times 100.$$

In the backcross generation 130 waltzers and 251 nonwaltzers were secured. The discrepancy from the expected 190.5 ± 9.8 of each type may be caused in part by errors in classification, in part by the fact that some animals included in the normal class may have been waltzers genotypically, and in part by the effects of the outcrosses which were involved in the production of some of the backcross young. As stated above, less than the expected number of homozygotes sometimes occurs after an outcross.

When only those backcross animals in which no outcross is involved are considered, and when the correction for 14.4 per cent of normal overlaps is made, the expected numbers (43.7 waltzers + 58.3 normals) are almost those which were actually secured (Table V). The numbers of each class in the backcross generation seem to correspond very closely to the numbers expected from a single recessive gene mutation.

TABLE V

INHERITANCE OF WALTZING (W) IN *P. MANICULATUS ARTEMISIAE* FROM PALOUSE RIVER, WASHINGTON

Number of defective and normal offspring from various types of matings and comparison with expected numbers, when waltzing is assumed to be a single unit recessive

Matings	Types Produced		Expected Types	
	ww	Ww+WW	ww	Ww+WW
ww × ww	71	12	83	0
Backcross				
Not outcrossed	43	59	51	51
Outcrossed to Palouse Falls	11	26	139.50	139.50
Outcrossed to Pullman	63	124		
Outcrossed to Polson	13	42		
Total backcross	130	251	190.50	190.50
F_2				
Not outcrossed	67	298	91.25	273.75
Outcrossed to Palouse Falls	16	95	40.25	120.75
Outcrossed to Polson	4	46		
Total F_2	87	439	131.50	394.50

The total numbers of backcross young derived from outcrosses are 87 waltzers and 192 nonwaltzers, although 139.5 of each class would be expected on the basis of a single recessive gene. Corrected for 14.4 per cent normal overlaps, the expected number differs from the number secured by 3.9 times the standard error. There is thus a deficiency over and above that caused by normal overlaps. This deficiency is doubtlessly the effect of the outcross, probably because of differences in the modifying factors present in different populations. Although the Palouse Falls station is only 5 miles from the Lyons Ferry station, the deficiency following this outcross is just as great as that following an outcross to *artemisiae* from Polson, which is several hundred miles from Lyons Ferry.

In the F_2 generation, 87 waltzers and 439 nonwaltzers were secured. For a single Mendelian recessive factor 131.5 ± 9.9 waltzers and 394.5 ± 9.9 nonwaltzers were expected. When the correction of 14.4 per cent for normal overlaps was applied, 112.5 waltzers and 413.5 nonwaltzers were then expected. The difference between the expected and obtained numbers is 4.5 times the standard error, and the difference between the numbers obtained and the corrected expected numbers is 2.6 times the standard error.

Of the F_2 animals not derived from an outcross, the difference between the actual numbers of the waltzing and nonwaltzing classes secured and the corrected expected numbers of the two types is only 1.3 times the standard error and is therefore not significant.

Twenty waltzers and 141 nonwaltzers, F_2 animals, were secured from outcrosses. The expected numbers, corrected for 14.4 per cent of normal overlaps, differ from the numbers produced by 2.6 times the standard error.

The data presented indicate that waltzing is recessive and is probably caused by a single gene mutation with modifying factors which produce normal overlaps. When no outcross is involved the numbers of waltzers and nonwaltzers are very close to expectation. When an outcross is involved the deficiency of the waltzing class is large. This may be accounted for by the probability that the outcross stock may have modifying factors which differ from those in the Palouse River stock.

When epilepsy is considered apart from the waltzing with which it is often associated in *Peromyscus maniculatus artemisiae,* it is found to be recessive in inheritance. The numbers of epileptics and nonepileptics obtained correspond fairly closely to those expected for a simple Mendelian recessive character.

Matings of epileptics by epileptics, however, produce both epileptics and nonepileptics (Table VI). Because individual defective animals differ greatly in their reactions, and because there is also a large range of variability in the reactions of an individual mouse tested at different times, it is very probable that some of these normally reacting mice are actually homozygous but fail to exhibit epileptic behavior when tested. Several of these

TABLE VI

INHERITANCE OF EPILEPSY (p) IN *P. MANICULATUS ARTEMISIAE*, FROM PALOUSE RIVER, WASHINGTON

Number of defective and normal offspring from various types of matings, and comparison with expected numbers, when epilepsy is assumed to be a single unit recessive

Matings	Types Produced		Expected Types	
	pp	Pp + PP	pp	Pp + PP
pp × pp	184	12	196.00	0.00
Backcross				
Not outcrossed	52	43	47.50	47.50
Outcrossed to Palouse Falls	24	59	69.00	69.00
Outcrossed to Polson	21	34		
Total backcross	97	136	116.50	116.50
F_2				
Not outcrossed	55	201	64.00	192.00
Outcrossed to Palouse Falls	20	91	40.25	120.75
Outcrossed to Polson	11	39		
Total F_2	86	331	104.25	312.75

normal animals are being tested at the present time by mating them with epileptic animals, but thus far no young have been produced. Since the twelve normals produced by matings of epileptics should have been epileptics, for convenience they may be considered to be normal overlaps. By using the formula

$$\frac{\text{Expected epileptics} - \text{Observed epileptics}}{\text{Expected epileptics}} \times 100$$

for the calculation of the percentage of normal overlaps, it is found that there are on the average 6.1 per cent normal overlaps for epilepsy. A correction of 6.1 per cent may therefore be used in calculating the expected numbers of epileptics.

In the backcross generation, there have been produced 97 epileptics and 136 nonepileptics. The theoretical expectation for this number of individuals for a simple Mendelian recessive character is 116.5 ± 7.6 epileptics and 116.5 ± 7.6 nonepileptics. When the expected numbers are corrected for normal overlaps, the corrected expected numbers of the two types are 109.4 epileptics and 123.6 nonepileptics. The difference between the corrected expected numbers and the actual numbers is only 1.6 times the standard error and is insignificant.

In the F_2 generation 86 epileptics and 331 nonepileptics have been secured. The expected numbers for one pair of allelomorphic characters are 104.25 ± 8.8 of the affected class and 312.75 ± 8.8 of the nonaffected class. If the correction for 6.1 per cent of normal overlaps, as explained above, is made, the expected numbers, 97.9 affected and 319.1 nonaffected, are close to the actual numbers secured.

The breeding data for the backcross and F_2 generations show very clearly that epilepsy is inherited in *P. m. artemisiae* as a single recessive gene mutation. When the correction for 6.1 per cent of normal overlaps is applied to the expected numbers, they are very close to the actual numbers of epileptics and nonepileptics produced. In every instance in which no outcross is involved the difference between the two is insignificant, but when an outcross is involved, the difference is somewhat larger, owing to the influence of the outcross. It appears then that in epilepsy in this subspecies modifying factors cause about 6.1 per cent of normal overlaps.

It is certain, as shown above, that both the epilepsy and waltzing of the Palouse River *artemisiae* are derived from the Lyons Ferry stock, though they may or may not have originated at the same time. At present, epilepsy and waltzing are almost inextricably intermingled in the descendants of this stock, and attempts to separate the two defects, if they are not identical in heredity, have so far resulted in failure.

When epilepsy and waltzing are considered together, the results are not as clear as they are when each defect is considered independently. Epilepsy and waltzing, though both are recessive in inheritance, do not segregate in a typically independent manner (see Table VII).

Matings of epileptic waltzers by epileptic waltzers have produced forty-three epileptic waltzers, ten epileptic nonwaltzers, and three nonepileptic waltzers. The animals which were not epileptic waltzers may have been misclassified or may have outgrown the abnormal behavior before the time of first testing. Since the variability of the reactions of epileptic and waltzing mice is very great, almost every mouse was tested at least three times before it was classified, and therefore it seems that most random errors should have been corrected by repeated tests. Some animals showed their abnormal behavior at the age of one month, but not thereafter, and it is possible that animals which exhibited the epileptic and waltzing characters very early in life already appeared normal with regard to one or other of these at the age of first testing, which is one month. The percentage of normal overlaps for waltzing is 17.9 and for epilepsy is 5.4 when the two characters are considered together. These percentages are very close to the 14.4 per cent of normal overlaps for waltzing and 6.1 per cent for epilepsy secured when the two types of behavior are considered separately. No apparently normal animals were produced from the mating of epileptic waltzer by epileptic waltzer. It is assumed, therefore, that there are no double overlaps, that is, there were no animals which should have been epileptic waltzers, yet phenotypically showed neither of the characters. In reality if a greater number of young had been produced in this cross, it is quite probable that there would have appeared some double overlaps, and in several other types of matings double overlaps actually may have occurred.

Since it was found in almost every cross that there were types of individuals produced other than those expected, an attempt has been made to determine whether these aberrant individuals were genetically different from their phenotype. Many of these individuals have failed to produce young, but there has been one very prolific animal. An epileptic nonwaltzing daughter of two epileptic waltzers should have been homozygous for both epilepsy and waltzing and, from breeding tests, appeared to be so.

Some epileptic waltzing animals were outcrossed to normal animals of several stocks of the same subspecies, *artemisiae,* to determine how the characters would segregate in the backcross and F_2 generations.

An outcross to *artemisiae* from Palouse Falls, in the backcross generation, produced nine epileptic waltzers, fifteen epileptic nonwaltzers, four nonepileptic waltzers, and fifty-five normals. After an outcross to the Polson stock, eleven epileptic waltzers, ten epileptic nonwaltzers, two nonepileptic waltzers, and thirty-two normals were produced.

In the F_2 generation ten epileptic waltzers, ten epileptic nonwaltzers, six nonepileptic waltzers, and eighty-five normals were derived from an outcross to *artemisiae* from Palouse Falls; three epileptic waltzers, eight epileptic nonwaltzers, one nonepileptic waltzer, and thirty-eight normals were the result of an outcross to *artemisiae* from Polson; and one epileptic waltzer, one epileptic nonwaltzer, one nonepileptic waltzer, and three normals were de-

TABLE VII

INHERITANCE OF EPILEPSY AND WALTZING IN *P. MANICULATUS ARTEMISIAE* FROM PALOUSE RIVER, WASHINGTON

Matings	Types Produced				Hypothesis	Expected Types				
	Normal	Epil.	Waltzer	Epil. Waltzer		Normal	Epil.	Waltzer	Epil. Waltzer	Total Defectives
Epileptic waltzer × epileptic waltzer	0	10	3	43	1 gene	0	....	....	....	56
					2 genes	0	0	0	56	
B.C. Epil. waltzer × F_1 (epil. waltzer × normal) outcrosses	87	25	6	20	1 gene	69.0 ± 5.9	....	....	....	69.0 ± 5.9
					2 genes	34.5 ± 5.1	34.5 ± 5.1	34.5 ± 5.1	34.5 ± 5.1	
F_2 (Epil. waltzer × normal) outcrosses	126	19	8	14	1 gene	125.25 ± 5.6	....	....	....	41.75 ± 5.6
					2 genes	94.0 ± 6.4	31.3 ± 5.8	31.3 ± 5.8	10.4 ± 3.1	
Epil. nonwaltzer × epil. nonwaltzer	2	46	0	13	1 gene	0	....	....	....	61
					2 genes	0	45.75 ± 3.4	0	15.25 ± 3.4	

rived from an outcross to a mutant *maniculatus* stock. If one gene only is involved in the inheritance of epilepsy and waltzing, the expected numbers are very close to the actual numbers secured.

The excess of normal and of epileptic waltzers may suggest the possibility of linkage between two separate hereditary factors. The class of epileptic nonwaltzers, which would be a crossover class is, however, larger than the class of epileptic waltzers, a noncrossover class. This occurs both in the backcross and in the F_2 ratios and seems to preclude the possibility of linkage between epilepsy and waltzing.

It seems most likely, therefore, that epilepsy and waltzing in *artemisiae* are both caused by the same major factor, but it is also probable that there are inherited modifying factors present, so that the offspring of epileptic nonwaltzer by epileptic nonwaltzer, for example, would show a higher proportion of epileptic nonwaltzers than of the other two possible pathological classes.

Epilepsy and Waltzing in artemisiae from Polson

One animal in the stock of *Peromyscus maniculatus artemisiae* from Polson, Montana, has exhibited both the epileptic and waltzing types of behavior. The animal, ♂ 19127, was first noted when it had an epileptic seizure after being disturbed in its cage. Although the animal was watched frequently, it was never observed to have another seizure. It was tested with the key-shaking machine and with other noises but did not show any epileptic behavior. The animal, however, waltzed frequently when disturbed by movement of its cage, when put into a new cage, or when stimulated by the key-shaking machine. The mouse is now 30 months old and still waltzes vigorously. There is little if any head movement.

The epileptic waltzing animal was mated with several of its daughters, and to date eleven offspring have been produced, all of which are normal in their reactions. Whether the epileptic and waltzing characters of this mouse are inherited or not is therefore unknown.

TYPES OF EPILEPSY IN *PEROMYSCUS*

Epilepsy occurs in five distinct stocks of *Peromyscus*. In three of these stocks, which represent two species and two species-groups, it is not associated with waltzing.

Epilepsy in rufinus

The seizures which occur in *Perimyscus maniculatus rufinus* from Deadman Flat, Arizona, are caused by the smoke of tobacco, oily rags, cotton, or incense. The noise from shaking keys or from a bell apparently does not affect the *rufinus* epileptics in any way.

When an epileptic *rufinus* is in the presence of any of these smokes it will usually stand on its hind legs and gradually fall over on its back; this is repeated several times, after which there ensues a period of bouncing in which the animal throws itself about violently for 10 to 15 seconds. If the smoke stimulus is removed, the animal gradually becomes quiet and remains motionless for a few minutes. The behavior thereafter is perfectly normal.

Epileptic animals of the *rufinus* stock react to the stimulus of smoke throughout life. The reactions of the old animals seem to be as vigorous as are those of the young mice. These epileptics appear to hear at all ages; ♀15722 still gave an ear twitch to the sound of a sharp noise at the age of 36 months.

Epilepsy in the *rufinus* stock is recessive in inheritance. Matings of epileptic by homozygous normals have produced thirty-nine normal young. In the F_2 generation eighty-two normals and six epileptics have been secured. There have been no backcross young produced as yet. The F_2 ratio suggests that there may be two recessive genes responsible for the appearance of epilepsy in *rufinus*. The number of normals and epileptics is very close to a 15 : 1 ratio, which for the number of young produced is 82.5 ± 2.3 normals and 5.5 ± 2.3 epileptics. The numbers, however, are still too few to determine certainly whether there are one, two, or more genes that determine the occurrence of the epilepsy.

All the normals and epileptics of the Deadman Flat stock of *rufinus* are the direct descendants of three field-caught animals, all of which must have been heterozygous for the epileptic gene or genes.

Epilepsy in osgoodi

Epilepsy occurs also in *Peromyscus maniculatus osgoodi* from Glen Ullin, North Dakota. The epileptic behavior of the *osgoodi* mice is almost identical with that of epileptic *artemisiae.*

The first epileptic animal noted was an old male, which died before it could be tested very extensively. The animal had numerous offspring, however, so that ten pairs of F_1's could be mated. Thus far ninety-four F_2's have been secured, of which ninety-three were normal and one was epileptic. This one epileptic animal was a female and when mature was backcrossed to her father. Up to the present five backcross young have been produced, of which four are normal and one epileptic.

Epilepsy in *osgoodi* is obviously recessive in inheritance, but it is impossible to say how many genes are responsible for its expression.

Epilepsy in rowleyi

Another type of epilepsy occurs in the stock of *Peromyscus boylii rowleyi* from Summerhaven, Arizona. The epileptic seizures are induced by any disturbance of the mouse, such as is caused by putting it into a clean cage. Though the *rowleyi* epileptics become very excited when tested with the shaking of keys, in only one instance was a seizure induced by this stimulus. Smoke does not affect the epileptic animals of this stock.

The epileptic seizures are of several types. In one type the animal falls on its side, beats its legs in clonic contractions, and then lies flat on its ventral side, with no control over its legs or body. In another kind of seizure the animal falls on its side, and is stiff for several minutes; it may lie in whatever position it happens to assume. In one instance, an animal lay with its body twisted so that its forelegs were on the floor and its hind legs extended straight up in the air.

Epilepsy in *P. b. rowleyi* is recessive in inheritance. Matings of epileptics by normals have produced twenty-four normal offspring. There have been sixty-five young produced in the F_2 generation, of which three were epileptic and sixty-two were normal. This is close to a 15:1 ratio, which for this number of animals would be 4.1 ± 1.95 epileptics to 60.9 ± 1.95 normals. The number of young produced, however, is too few to determine certainly whether epilepsy in *P. b. rowleyi* is caused by one, two, or more genes.

All the animals of the stock of *rowleyi* from Summerhaven have been derived from four field-caught animals, and the epileptic animals have appeared in the second and third inbred generations. The gene or genes for epilepsy must, therefore, have been present in the field-caught animals.

OTHER NERVOUS DISORDERS IN *PEROMYSCUS*

Almost all the nervous disorders that occur in *Peromyscus* may be roughly classed as epilepsy or as waltzing. There is one nervous defect, however, which does not fall typically into either of these classes. Huestis and Barto (1936: 438) have described an inherited tremor in *Peromyscus* "characterized by trembling of the limbs and body and accompanied by deficient growth and . . . death before five weeks of age."

DISCUSSION

The epilepsy in *Peromyscus* is very similar to idiopathic epilepsy in man. The clonic and tonic phases of the seizure and the gradual recovery, followed by exhaustion and drowsiness, are almost identical in *Peromyscus* and in man. Although the literature on the inheritance of epilepsy in man is voluminous, little positive information about the mode of inheritance of the defect has been secured. Part of the difficulty is that epilepsy is probably a symptom of many mental and physical disorders and is not a disease entity. Some writers find a very high incidence of epilepsy in the families of epileptics, but others find just the opposite. Some writers have found that epilepsy is associated in inheritance with migraine, feeblemindedness, and other disorders, and others find that it is independent in heredity. These differences in results are probably due, at least in part, to differences in the types of epilepsy studied by the different authors. In *Peromyscus* the various types of epilepsy occur in different stocks, so that each type may be studied separately.

Epilepsy in *P. maniculatus artemisiae* is also similar in some respects to Ménière's syndrome complex in man, with its attendant deafness.

It has been demonstrated clearly in the study of epilepsy and waltzing in *Peromyscus* that somewhat similarly appearing defects may be caused by different hereditary factors. The two types of waltzing in the stocks of *bairdii* and of *artemisiae,* respectively, have been shown to be different in heredity. Likewise, the two types of epilepsy occurring in *artemisiae* and in *rufinus,* respectively, are certainly distinct in view of the difference in expression of the character and in the stimulation necessary to produce the typical epileptic reactions.

It is significant that epilepsy and waltzing were carried in heterozygous condition by the field-caught *Peromyscus,* for the defects appeared after one or more generations of inbreeding in the laboratory. In all cases which could be tested, the defect did not result from the laboratory environment. Homozygous epileptic or waltzing animals no doubt would usually be eliminated in nature by their failure to escape in time of danger.

SUMMARY

Waltzing and epilepsy have appeared independently in nine different stocks of *Peromyscus* kept at the Laboratory of Vertebrate Genetics of the University of Michigan.

Waltzing is recessive in each of the five stocks in which the mode of inheritance has been determined, and in each case, it appears to be due to a single recessive gene.

Epilepsy, likewise, is recessive, and in the *Peromyscus maniculatus artemisiae* stock from Palouse River, it is caused by one recessive gene, but in the stocks of *P. m. osgoodi, P. m. rufinus,* and *P. boylii rowleyi* it may be the effect of one, two, or more recessive genes.

When waltzing and epilepsy occur together in the same stock, as in *P. m. artemisiae* from Palouse River, the mode of inheritance of the characters is less clear. Each is recessive when considered alone, but when epilepsy and waltzing are considered together, they do not segregate in a typically independent manner, yet they do not appear to be caused by linked genes. It is suggested that both defects are the result of one major factor, but that inherited modifying factors affect the expression of the character. Epilepsy yields to selection, in that promptly-reacting parents produce a majority of promptly-reacting offspring, and slowly-reacting parents produce a majority of slowly-reacting offspring.

The epileptic behavior of *Peromyscus maniculatus artemisiae* from Palouse River is extremely variable. The epileptic reaction may be a complete seizure, a bouncing seizure, stupor, semistupor, or dashing. Sound stimuli of various kinds will produce the epileptic reactions. The reactions of epileptic mice vary with the age of the animal when tested and with the intensity and duration of the stimulus. Within the limits set in this study, the louder the stimulus or the longer the duration the more severe is the epileptic reaction. Individual mice vary from time to time in their reactions,

even when tested with the same stimulus. This variation in response is probably caused by changes in the physiological condition of the animal.

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